DETAILED ACTION

Claim Status

1. Claims 1-13, 16 and 22 have been canceled as filed on 6/27/2007.

Claim 25 has been added as filed on 1/8/08.

Claims 14, 15, 17-21 and 23-25 are currently pending as filed on 1/8/08.

Claims 19-21 have been withdrawn as previously acknowledged.

Claims 14, 15, 17, 18 and 23-25 are being examined in this application.

Election/Restrictions

2. Applicant's election with traverse of Group 1 (Claims 14-18) over the telephone has been previously acknowledged (see the previous Office action, mailed 3/13/06, pp. 4-5).

3. Applicants has added claim 25 as filed on 1/8/08, which the newly added claim is grouped together with Group I invention, and are thus examined in the instant application.

4. Applicants elected with traverse of the following species as previously acknowledged:

A.) ERGIC-53;

B.) membrane bound protein;

C.) "D-Gal".

Priority

5. Applicant's filing of a translation (filed on 7/12/06) for the Foreign application: JAPAN 2002-238559; filed on 8/19/2002) is as previously acknowledged.

Claim Objection(s) / Rejection(s) Withdrawn

6. In light of applicant's amendment to the instant claim 24, the following objection is withdrawn:

Claim 24 is objected to because of the following informalities: The instant claim 17 from which Claim 24 depends on as well as Claim 24 recites "A plurality of eukaryotic cells" in plural, however, the instant claim 24 recites "said cell is". Appropriate correction is required.

Claim Objection(s) / Rejections Maintained

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

Ueno

8. Claims 14, 17, 18, 23 and 24 are rejected under **35 U.S.C. 102(b)** as being anticipated by Ueno et al (Nihon Yakugakkai Dai 121 nenkai Yoshishu, Page 9; Issued on March 5, 2001; Abstract for a meeting of the Pharmaceutical Society of Japan; Cited in IDS). The previous rejection is maintained for the reasons of record as set forth in the Office action as well as the discussion below.

The instant claims recites eukaryotic cell comprising heterologous DNA coding for a mutant of the native cargo receptor ERGIC-53 represented by SEQ ID No:2 or VIP36 represented by SEQ ID NO: 4, wherein the mutant comprises an alteration of at least one amino acid, relative to the native cargo receptor, wherein the alteration is in the sequence of the native cargo receptor's carbohydrate recognition domain, between amino acid residues 152 and 160 of SEQ ID NO: 2, exclusive of the conserved residues at positions 152 and 156, or between amino acid residues 162 and 170 of SEQ ID NO: 4, exclusive of the conserved residues at positions 162 and 166 such that (i) said cell expresses a glycoprotein with a modified carbohydrate moiety comprising at least one glycoform selected from the group consisting of D-Gal, D-Man, D-Glc, D-GlcNAc, L-Fuc, SA, and D-GalNac; and (ii) the modified cargo receptor is capable of selectively transporting the glycoprotein in said cell.

Ueno et al teach generation of eukaryotic cells (MDCK cells) comprising ERGIC-53 with altered lectin domains (carbohydrate binding domains), which reads on the eukaryotic animal cells of **clms 14, 23 and 24**. (See the entire abstract) The reference teaches the ERGIC-53 cDNA was altered at its lectin domain (reads on alteration of its carbohydrate recognition domain) (See 2nd paragraph of the reference.). The ERGIC-53 cargo receptor has an amino acid sequence matches the instant SEQ ID No:2, and is homologous to the VIP36 cargo receptor with an amino acid sequence matches the instant SEQ ID NO:4. In addition to the mutants of ERGIC-53, the wild-type ERGIC-53 would read on a cargo receptor with "an alteration of at least one amino acid, relative to a native cargo receptor, where in the alteration is in the sequence of the native cargo receptor's carbohydrate recognition domain… between amino acid residues 162 and 170 of SEQ ID NO:4, exclusive of the conserved residues at positions 162 and 166". As

indicated in the attached Sequence Alignment Result between ERGIC-53 (SEQ ID NO:2) and VIP36 (SEQ ID NO:4) (Alignment by BLAST, Result downloaded from http://www.ncbi.nlm.nih.gov/blast/bl2seq/wblast2.cgi?0; 9/1/07; cited previously), the ERGIC53 cargo receptor would have alteration of at least one amino acid between the amino acid residues 162 and 170 of SEQ ID NO:4. For example, amino acid residue 154 of ERGIC53 is "altered" "relative" to the "native cargo receptor", VIP36 (or the instant SEQ ID NO:4), and residues 152 and 160 of ERGIC53 are not "altered" "relative" to the residues 162 and 166 of VIP36.

The reference further teaches the said ERGIC-53 cDNA was inserted into a plasmid and expressed in mammalian cells (reads on eukaryotic cell comprising heterologous DNA coding for a cargo receptor). (See 2nd paragraph) These read on the cargo receptor encoded by the heterologous DNA of **clm 14.**

The reference also teaches that various alterations to the lectin domain were created and that "various recombinants ERGIC-53" were transfected into mammalian cells to "obtain various cell lines" (2nd paragraph), which reads on a plurality of eukaryotic cells expressing a variety of carbohydrate recognition domains, as recited in **clm 17**.

The reference further teaches that "a glycoprotein having distinctive glycoform was observed in some of the recombinants ERGIC-53" (see 3rd paragraph), which reads on eukaryotic cells expressing glycoprotein with a particular glycoform, as recited in **clm 18**.

The reference also teaches BPA lectin binds to galactose (para 2), which reads on the glycoform (D-Gal) of **clm 14**. Furthermore, the recitations of "wherein said plurality is enriched for eukaryotic cells that express glycoprotein characterized by a particular glycoform" (the instant Claim 18) is construed as intended use of the claimed product. As discussed above, the

eukaryotic cell comprising the cargo receptor is structurally the same as the claimed product, and thus, the cargo receptor taught by the reference is capable of performing the intended function of binding to D-Gal glycoform, as recited in **clm 18**.

In addition, the eukaryotic cells also inherently comprise glycoproteins with D-Gal glycoform as recited in **clm 14**, as evidenced by the instant specification. The instant specification states that the eukaryotic cells are transfected with DNA encoding for mutant "cargo receptors" such as ERGIC-53 mutants, and then isolate cells based on glycoproteins with particular glycoforms (see Examples 1-11, especially, Example 10 of the instant spec.). That is the eukaryotic cells inherently possess glycoproteins with different glycoforms such as D-Gal. For example, Table 5, for example, shows the different glycoforms (including D-Gal) comprised by the eukaryotic cells.

Discussion and Answer to Argument

9. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the cited reference does not teach all element of the claimed invention. Applicants argue the instant "claim 14 has been amended accordingly to explicitly recite the mutants of the cargo receptor ERGIC-53 ***and*** *VIP-36, relative to their native counterparts, thereby obviating the stated rationale for the rejection." (Emphasis added; Reply, p.5, para 1).*

First, it is noted that the amended claim (claim 14) recites "ERGIC-53… **or** VIP36" in the alternative.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "the mutants of the cargo receptor ERGIC-53 and VIP-36") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants also argue that the mutations where BPA or MAH lectin domains was recombined with the ERGIC-53 receptor do not read on the instant claimed mutant receptors. However, as discussed previously and above, the recombinant ERGIC-53 expressed in the MDCK cells is a "mutant" relative to the wild-type VIP36 amino acid sequence. As discussed above, the ERGIC-53 amino acid sequence has amino acid substitution mutations relative to the wildtype VIP36 protein between positions 162-170.

Applicants also argue the "chimeric ERGIC-53 protein disclosed by Ueno does not retain the function of being capable of transporting glycoproteins selectively in eukaryotic cells," because "the chimeric proteins remain localized in Golgi and cannot be mobilize into the cytoplasm." (Reply, pp.5-6).

First, the said "mobilize into the cytoplasm" is not a feature recited in the instant claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., capable of mobilizing into the cytoplasm) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Second, applicants are arguing the intended use of the claimed product. The Ueno reference teaches all required structural elements of the claimed product. In response to applicant's argument that the reference does not teach the cargo receptor is capable of selectively transporting the glycoprotein in said cell, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

In this case, the Ueno reference teaches the cargo receptors are localized to the ER and the Golgi apparatus (Ueno, para 2), which organelles (ER and Golgi) are the site for processing and transporting glycoproteins, as evidenced by the instant specification. The instant disclosure states "after being synthesized in a form having carbohydrates added in the ER within eukaryotic cells, carbohydrate moieties (sugar moieties) of glycoproteins are subjected to processing in the Golgi …" (Spec. [0042]). Thus, the cargo receptors of the Ueno reference would be capable of performing the intended use of "transporting the glycoprotein in said cell".

Applicants also assert the phrase "is capable of selectively transporting the glycoprotein in said cell" is not "intended use" language, rather the said phrase provides "a functional limitation". However, the "functional limitation" must result in structural difference to render patentable weight for the claimed product. (see MPEP 2114). As discussed above, the cargo-receptor of the reference is shown to be capable of performing the recited function as well as structurally the same to the instant claimed product. Thus, the reference anticipates the claimed invention.

Hirai

10. Claims 14, 15, 17, 18, 23 and 24 are rejected under **35 U.S.C. 102(b)** as being anticipated by Hirai et al (Nihon Yakugakkai Dai 121 nenkai Yoshishu, Page 7; Issued on March 5, 2001; Abstract for a meeting of the Pharmaceutical Society of Japan; Cited in IDS). The previous rejection is maintained for the reasons of record as set forth in the Office action as well as the discussion below.

Hirai et al teach the generation of recombinant VIP36 containing MDCK cells (read on the animal cells of the instant claims 23 and 24) (See the entire document). The reference teaches that the lectin domain (carbohydrate binding domain) of VIP36 (cargo receptor) was recombined with BPA lectin and MAH lectin (would read on a variety of carbohydrate recognition domain and alteration of the said domain). The reference also teaches the cells used to express the recombinant VIP36 mutants are MDCK cells (would read on a eukaryotic cells). The reference further teaches observing "the structural and functional changes in sugar chains of glycoproteins to be biosynthesized" in the cells comprising the altered carbohydrate recognition domain (See 1st paragraph), which would read on the intend use of expressing glycoprotein with modified carbohydrate moiety. In addition, the reference teaches that the cells having the different chimeric or recombinant cargo receptor expressed therein specific types of sugar chains of intracellular and extracellular glycoproteins (See last paragraph), which would read on a plurality of cells expressing glycoprotein with a particular glycoform. Furthermore, the reference teaches the intracellular and extracellular localization of the expressed glycoprotein using FACS analysis, which would read on membrane-bound or secretory protein.

The ERGIC-53 cargo receptor has an amino acid sequence matches the instant SEQ ID No:2, and is homologous to the VIP36 cargo receptor with an amino acid sequence matches the instant SEQ ID NO:4. In addition to the mutants of VIP36, the wild-type VIP36 would read on a cargo receptor with "an alteration of at least one amino acid, relative to a native cargo receptor, where in the alteration is in the sequence of the native cargo receptor's carbohydrate recognition domain… between amino acid residues 152 and 160 of SEQ ID NO:2, exclusive of the conserved residues at positions 152 and 156". As indicated in the attached Sequence Alignment Result between ERGIC-53 (SEQ ID NO:2) and VIP36 (SEQ ID NO:4) (Alignment by BLAST, Result downloaded from http://www.ncbi.nlm.nih.gov/blast/bl2seq/wblast2.cgi?0; 9/1/07), the VIP36 cargo receptor would have alteration of at least one amino acid between the amino acid residues 152 and 160 of SEQ ID NO:2. For example, amino acid residue 164 of VIP36 is "altered" "relative" to the "native cargo receptor", ERGIC53 (or the instant SEQ ID NO:2), and residues 162 and 166 of VIP36 are not "altered" "relative" to the residues 1152 and 156 of ERGIC53.

The recitations of "wherein said plurality is enriched for eukaryotic cells that express glycoprotein characterized by a particular glycoform" (the instant Claims 18, 23 and 24) is construed as intended use of the claimed product. As discussed above, the eukaryotic cell comprising the cargo receptor is structurally the same as the claimed product, and thus, the cargo receptor taught by the reference is capable of performing the intended function of binding to D-Gal glycoform.

In addition, the eukaryotic cells also inherently comprise glycoproteins with D-Gal glycoform, as evidenced by the instant specification. The instant specification states that the

eukaryotic cells are transfected with DNA encoding for mutant "cargo receptors" such as VIP36 mutants, and then isolate cells based on glycoproteins with particular glycoforms (see Examples 1-12, especially, Example 12 of the instant spec.). That is the eukaryotic cells inherently possess glycoproteins with different glycoforms such as D-Gal. For example, Table 5, for example, shows the different glycoforms (including D-Gal) comprised by the eukaryotic cells.

Discussion and Answer to Argument

11. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants have traversed the rejection over the Hirai reference with the same arguments as the Ueno reference.

Applicant's are respectively directed to the above discussion under Ueno for answer to arguments.

Applicants also repeated the previous arguments of using the Takimori paper as evidence to indicate "the chimeric VIp-36 protein of Hirai does not have the function of being capable of transporting glycoproteins selectively in eukaryotic cells." (Reply, p.7, para 3).

As discussed previously, Applicants have not demonstrated how the cargo receptors of Ueno reference are equivalent to the cargo receptors of the Takimori reference. It is not clear how the results of the Takimori reference would correlate to the cargo receptors for the Ueno reference.

Furthermore, the recitation of Takimori cited by applicants (i.e. "last six lines of at page 2") does not clearly support applicant's assertion. The recitation seems to indicate that the cargo receptors can be observed in different locations within the cells, but not incapable of transporting glycoproteins.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Itin and Yamamoto

13. Claims 14, 15, 17, 18, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Itin et al (Molecular Biology of the Cell. Vol. 7: 483-493; 1996; cited in IDS), in view of Yamamoto et al (Journal of Biochemistry. Vol. 127: 137-142; 2000; cited in IDS). The previous rejection is maintained for the reasons of record as set forth in the Office action as well as the discussion below.

Itin et al, throughout the publication, teach modifying the carbohydrate binding region of ERGIC-53 and expressing the wildtype as well as the modified lectin in eukaryotic cells (e.g. Abstract). The reference teaches that the modified protein is overexpressed in COS-1 cells (which are eukaryotic animal cells; See page 485 left col. 2nd paragraph). These teachings read

on the eukaryotic animal cells or plurality of eukaryotic cells comprising a cargo receptor, as recited in **clms 14, 23 and 24**.

The reference also teach the ERGIC-53 cargo receptor share homology to other lectins, and the region encompassing amino acid residues from position 117 to position 158 is the carbohydrate binding domain (e.g. Figure 1).

Itin et al do not explicitly teach "an alteration of at least one amino acid, relative to a native cargo receptor… between amino acid residues 152 and 160 of SEQ ID NO:2", as recited in **clm 14**. The reference also does not explicitly teach the intended use of "enriched for" "a particular glycoform", as recited in **clm 18**. The reference also does not explicitly teach the inherent properties of "expresses a variety of glycoproteins", and the "glycoprotein is a membrane-bound protein or a secretory protein", as recited in **clms 17 and 15**.

However, Yamamoto et al, throughout the reference, teach mutating lectins at their carbohydrate binding domains to produce lectins (or cargo receptors) with altered carbohydrate binding specificities (Abstract). The reference also teaches the mutated lectins bind to various carbohydrate groups such as GalNAc (e.g. p. 138, col.2, para 4). The reference also teaches the need to make artificial lectins with desired carbohydrate binding specificities such as to study the mechanism of carbohydrate binding (e.g. p. 137, col.1-2; especially, col.2, para 3; p.141). The reference also teaches the specific amino acid sequence that is important for carbohydrate binding (DTWPNTEWS) (e.g. p.137, col.1; Figure 4). The reference teaches the amino acid sequence alignment of lectins such as EcorL and LOL to indicate the carbohydrate binding region such as the boxed region in Figure 4 of the reference. The reference also indicates that the "D" residue and the "N" residue are highly conserved among the various lectins (e.g. Figure 4).

The Yamamoto reference also teaches enriching cells for cargo receptor that would bind to certain carbohydrates (e.g. p.139, cols.1-2, bridging).

In addition, the Itin reference also provides an alignment of the carbohydrate binding domains of the EcoRL, LOL and ERGIC-53 lectins (See Figure 1 of the Itin reference). The alignment as shown in Figure 1 of Itin reference also indicates the specific carbohydrate binding regions of ERGIC53 (residues 152-156), LOL (residues 121-125), and EcoRL (residues 129-133), which regions share high homology. The Figure also shows the residues of positions 152 and 156 of ERGIC53 are highly conservative, as they are shown in the Yamamoto reference. The Itin reference also specifically teaches mutation at position 156 abolished carbohydrate binding (e.g p.487, col.2).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to make a eukaryotic cell comprising a cargo receptor having altered amino acid residues relative to a native cargo receptor such as ERGIC53 (SEQ ID NO:2) at the specific amino acid positions 152-160 excluding the highly conserved residues at positions 152 and 156, as well as enriching for a cargo receptor that selectively binds to the desired carbohydrate moiety.

A person of ordinary skill in the art would have been motivated at the time of the invention to make various mutations in the carbohydrate recognition region of a native cargo receptor such as ERGIC53, because the need to generate cargo receptors that can recognize novel or different carbohydrate moieties for various applications, as taught by Yamamoto et al.

In addition, the amino acid sequence of ERGIC53 (SEQ ID NO:2) is known in the art, and more importantly, its carbohydrate binding domain is known in the art, as taught by Itin et al.

The highly conserved amino acid residues in the carbohydrate binding domain among lectins are known and mutations among the non-conserved amino acid residues produced altered carbohydrate binding abilities, as taught by Yamamoto et al discussed above. Thus, one of ordinary skill in the art would substitute different amino acid residues at the known carbohydrate binding domains in ERGIC53 while avoiding the known conserved residues (at 152 and 156) for the predictable results of generating mutant ERGIC53 that would have altered carbohydrate binding ability.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since the method of generating various mutant cargo receptors with different carbohydrate binding abilities are known in the art, as demonstrated by both Itin et al and Yamamoto et al.

In addition, the cells comprising modified ERGIC53 or cargo receptors would inherently comprise the various glycoproteins that are membrane-bound, secretory, and possess a particular glycoform, as evidenced by the instant specification. The instant specification states that the eukaryotic cells are transfected with DNA encoding for mutant "cargo receptors" such as ERGIC-53 mutants, and then isolate cells based on glycoproteins with particular glycoforms (see Examples 1-11, especially, Example 10 of the instant spec.). That is the eukaryotic cells inherently possess glycoproteins with different glycoforms such as D-Gal. For example, Table 5, for example, shows the different glycoforms (including D-Gal) comprised by the eukaryotic cells.

Discussion and Answer to Argument

14. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants assert that "impermissible hindsight" was used to make the above obviousness rejection. (Reply, p.8, para 1).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicants also state that residue "D121" and "N152" are indicated as conserved residues, but not residue "D152" in Figure 1 of Itin. (Reply, p.8, para 3). Therefore, applicants conclude "one of skilled in the art would not have considered it obvious to… arrive at the mutant of the invention."

However, Figure 1 of the Itin reference also explicitly states "Underlined are conserved amino acids". As indicated in Figure 1, at least residues 152 and 156 are underlined.

Applicants also argue because of the "lower homology between ERGIC-53 cargo receptor and leguminous lectins", one of ordinary skill in the art would not be motivated to

"replace the specific domain of a cargo receptor with the corresponding domain of a plant lectin, or randomly to replace the specific domain of a cargo receptor". (Reply, p.8, last para).

Applicants are respectively directed to the above claim rejection on detailed discussion on the teachings of the references. Applicants have made the assertion regarding "homology" among the various proteins without providing supporting evidence. As indicated in Figure 1 of Itine and Figure 4 of Yamamoto, the amino acid residues between positions 152 to 156 of the ERGIC-53 and their corresponding sequences in plant lectins are highly conserved and are important for carbohydrate binding ability. From amino acid residues, positions 152 and 156 of the ERGIC-53 have highly conserved "D" and "N" residues for all of the aligned homologous sequences as indicated in Figure 1 of Itin and Figure 4 of Yamamoto. In addition, Yamamoto et al also demonstrated that mutation of any amino acid sequences in between the "D" and the "N" residues would alter the carbohydrate binding ability of the resulting lectin protein. Thus, it would have been obvious for one of ordinary skill in the art to mutate the in between residues while holding the highly conserved "D" and "N" constant.

New Claim Objections / Rejections

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

16. Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is necessitated by applicant's amendments to the claims.

Claim 25 has been added to recite "A eukaryotic cell according to claim 14, which does not express native receptor ERGIC-53 or VIP36" as filed on 1/8/08. However, the instant specification does not provide support for the claimed eukaryotic cell as recited in Claim 25. In particular, the instant specification and claims as originally filed do not disclose an eukaryotic cell that does not express the native receptor ERGIC-53 or VIP36.

Applicants have pointed to the "original specification, for example, at page 9, first full paragraph" for support of the newly added claim 9. The "first full paragraph" at page 9 of the instant specification is cited below:

"The present invention is characterized in that a carbohydrate recognition domain of a cargo receptor, particularly a carbohydrate-binding domain, is altered. In the present invention, the term "alteration of a carbohydrate recognition domain" means that when a cargo receptor is expressed as proteins, its carbohydrate recognition domain or its carbohydrate-binding domain differs from that of native one in terms of sequence and/or structure; or that a carbohydrate moiety (sugar chain) to be added differs from that of native protein to be expressed in cells. Hence, in addition to the above described specific sequences, alteration of a cargo receptor, whereby a carbohydrate moiety differing from that to be added before alteration, is also encompassed in the term "alteration of a carbohydrate recognition domain" according to the present invention."

The above cited paragraph of the instant specification provides a description of the term "alteration of a carbohydrate recognition domain". The said paragraph does not provides support for the claimed "eukaryotic cells" without a native ERGIC-53 or VIP36 receptor.

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claim 25 represents new matter.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. L./
Examiner, Art Unit 1639
3/31/08

/Jon D. Epperson/
Primary Examiner, AU 1639